

REMARKS

The Present Invention

The present invention is directed to a method of inhibiting binding of an enveloped virus to a cell in a host. The method comprises administering to the host an antiviral effective amount of an isolated and purified antiviral agent selected from the group consisting of an antiviral protein, an antiviral peptide, an antiviral protein conjugate, and an antiviral peptide conjugate, wherein said antiviral protein or antiviral peptide has an amino acid sequence of SEQ ID NO: 2 or an antiviral fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2, whereupon administration of said antiviral effective amount of said antiviral agent, binding of the enveloped virus to the cell is inhibited.

The Pending Claims

Claims 20-31 are currently pending and are directed to the method of inhibiting binding of an enveloped virus to a cell in a host.

The Office Action

The Office has rejected claims 22-31 under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description (claims 22-31) and/or lacking enablement (claims 20-30). Claims 20 and 21 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 20-24 of Application No. 09/428,275. Reconsideration of this rejection and this provisional rejection is hereby requested.

Discussion of Written Description Rejection

Claims 20-27 have been rejected under Section 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. This rejection is traversed for the reasons set forth below.

According to the Office, the instant application does not provide adequate support for claims involving the co-administration of cyanovirin and a virus or viral envelope protein. On the contrary, every feature of claims 22-31 is adequately described in the instant specification. For example, the instant application describes a method of inhibiting binding of a virus to a cell comprising administering to a host an antiviral peptide conjugate or an antiviral protein conjugate having an amino acid sequence of SEQ ID NO: 2 or a fragment thereof at, for example, page 4, lines 16-25, page 5, line 31, through page 6, line 4, page 21, lines 15-22,

and page 22, lines 7-20. Formulations and dosages of compositions comprising the antiviral peptide conjugate or antiviral protein conjugate also are described in the instant specification (see, for example, page 28, line 15, through page 29, line 14, and page 31, lines 18-34). The antiviral peptide conjugate or antiviral protein conjugate of the claimed method is further described at, for example, page 3, lines 27-29, page 12, lines 16-19, page 18, lines 24-36, and page 20, lines 19-25. An example of such an antiviral protein conjugate or an antiviral peptide conjugate, namely an antiviral protein conjugate or antiviral peptide conjugate comprising cyanovirin and a viral envelope glycoprotein or a virus, is described in, for instance, Examples 5 and 6.

In view of the above, the instant specification clearly describes a method of inhibiting binding of a virus to a cell using an antiviral peptide conjugate or antiviral protein conjugate, such as those recited in claims 22-31, and thereby adequately conveys that the inventor was in possession of the claimed invention at the time of filing of the instant application. Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 22-31 under Section 112, first paragraph, for alleged lack of written description.

Discussion of Enablement Rejection

Claims 20-31 have been rejected under Section 112, first paragraph, for alleged lack of enablement. This rejection is traversed for the reasons set forth below.

The courts have ruled that the Office bears the burden of demonstrating that a claimed invention is not enabled. See *In re Wright*, 999 F.2d. 1557, 1561-63, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993) (“When rejecting a claim under the enablement requirement of Section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application.”). In regard to the instant application, the Office contends that the claimed invention is not enabled in two respects: (1) the instant specification allegedly provides insufficient guidance as to which regions of the cyanovirin peptide are required for antiviral activity, and (2) the instant specification allegedly does not provide any *in vivo* working examples. In both respects, the Office has failed to meet its burden in demonstrating that undue experimentation would be required to make and use the present invention as claimed.

The pending claims recite that the antiviral protein or antiviral peptide of the claimed method has an amino acid sequence of SEQ ID NO: 2 or an antiviral fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2. Applicant has provided sufficient guidance to enable the ordinarily skilled artisan to make and use the antiviral protein, antiviral peptide, or antiviral fragment thereof by providing nucleic acid and amino

acid sequences encoding cyanovirins in SEQ ID NOS: 1-4 and Figure 2, for example. As required by the pending claims, the amino acid sequence of SEQ ID NO: 2 or the fragment thereof comprising at least nine contiguous amino acids of SEQ ID NO: 2 have antiviral activity. Methods of screening candidate proteins and peptides for antiviral activity are provided in the instant specification at, for example, page 24, line 19, through page 25, line 25, and in Examples 5 and 6. The methods involve routine laboratory techniques that are well within the skill of the ordinary artisan.

In response to Applicant's previous assertions that only routine experimentation would be required to generate and screen antiviral peptide fragments comprising at least nine contiguous amino acids of SEQ ID NO: 2, the Office merely states that "the Examiner does not concur with this assessment" and that it is purportedly well documented that mutations within amino acid sequences can have deleterious effects on the activity of a given protein or peptide (Office Action (Paper 18), page 6, lines 9-12). First, while some inoperative embodiments may be embraced by the claims, the pending claims need not be drafted to exclude such inoperative embodiments (see, e.g., M.P.E.P. 2164.08(b)). Second, the Office has failed to demonstrate that undue experimentation would be required to practice the present inventive method as claimed. Some required experimentation does not render a claimed invention non-enabled. See *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d. 1367, 1384, 231 U.S.P.Q.2d 81, 94 (Fed. Cir. 1987). See also *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976) ("The key word is 'undue,' not 'experimentation.'"). The generation of peptide fragments from a given nucleic acid or amino acid sequence and screening such peptide fragments for antiviral activity using methods provided in the instant specification cannot properly be considered as *undue* experimentation. The Office has not met its burden in demonstrating non-enablement.

The Office contends that the disclosure of the instant application "fails to provide any data suggesting that the claimed compositions would function in an *in vivo* setting," and, therefore, "is not enabled for *in vivo* inhibitory applications" (Office Action (Paper 18), page 5, lines 9-20). On the contrary, the instant specification provides sufficient guidance to enable the ordinarily skilled artisan to make and use the invention as claimed, and further provides data which demonstrate that cyanovirin inhibits binding of an enveloped virus to a cell *in vitro*. In addition, Applicant has provided convincing evidence that the composition of the claimed method functions *in vivo*.

The pending claims are directed to a method of inhibiting binding of an enveloped virus to a cell in a host. The pending claims do not require preventing or curing a disease. The instant specification teaches how to make and the isolated and purified antiviral agent at, e.g., page 10,

line 25, through page 13, line 19, page 14, line 8, through page 16, line 10, and page 18, line 24, through page 19, line 28. Methods of administering the isolated and purified antiviral agent to a host to inhibit binding of an enveloped virus to a cell are described at page 25, line 7, through page 26, line 32, page 27, line 30, through page 30, line 13, and page 31, line 18, through page 33, line 10. Examples 5 and 6 of the instant specification, as well as the data provided to the Office by way of the Declarations submitted August 3, 2001, and January 7, 2002, provide convincing evidence that cyanovirin inhibits binding of a number of enveloped viruses to cells in a host. However, in spite of the teachings of the specification and the provided evidence, the Office contends that *in vitro* assays are not predictive of *clinical* efficacy and cites numerous references which allegedly support this contention.

Many of the references cited by the Office are not probative of the predictability with which cyanovirin inhibits binding of an enveloped virus to a cell in a host. For example, Saunders (*Drug Design and Discovery*, 8, 255-263 (1992)) and Gait and Karn (*TIBTECH*, 13, 430-438 (1995)) are directed to non-nucleoside inhibitors and protease inhibitors, respectively, which have no effect on binding of a virus to a host cell. Richman (*Antiviral Chemotherapy*, 4, 383-395 (1996)) allegedly notes that HIV exists as a quasispecies in an infected patient. Again, the reference cited by the Office does not cast doubt on the predictability of cyanovirin in inhibiting binding of an enveloped virus to a cell in a host.

The Office contends that Oberg and Vrang (*Eur. J. Clin. Microbiol. Infect. Dis.*, 9(7), 466-471 (1990)) addresses limitations of tissue culture-based screening assays and disadvantages of animal models. Examples 5 and 6 of the instant application describe an *in vitro* assay employing lymphocytes. Using the macaque model described in the Declaration submitted February 5, 2001, peripheral blood monocytes (PBMCs) were isolated from blood samples to identify cells infected by virus. Thus, contrary to the assertion by the Office, Applicant has indeed demonstrated that cyanovirin inhibits viral binding to cells "that reflect the natural *in vivo* target" of HIV.

The remaining references cited by the Office pertain to agents that purportedly block viral binding to cells. According to the Office, the references support the contention that clinical activity is not guaranteed by *in vitro* assays. In this regard, the Courts have ruled that an invention is not required to be ready for clinical application to meet the requirements of patentability. See *In re Brana*, 51 F.3d. 1560, 1568, 34 U.S.P.Q.2d 1436, 1442 (Fed. Cir. 1995). However, in addition to the *in vitro* data provided in the specification of the instant application, Applicant has provided *in vivo* evidence confirming that cyanovirin inhibits viral binding to a cell by way of the Rule 132 Declarations submitted February 1, 2001, and January 7, 2002. The Office contends that the animal data provided in these Declarations are

insufficient as reductions in viral load and increases in CD4+ lymphocyte count are not verified and, therefore, the ordinarily skilled artisan allegedly cannot make a meaningful deductions pertaining to the therapeutic properties of the antiviral composition. Yet, all that is required by the pending claims is inhibition of binding of an enveloped virus to a cell in a host. The macaque model described in the Declaration of February 1, 2001, and the mouse model described in the Declaration of January 7, 2002, prove that the isolated and purified antiviral agent of the inventive method inhibits binding of an enveloped virus to a host cell *in vivo*. Demonstration of reductions in viral load or increases in lymphocyte count is not required in the context of the presently claimed inventive method, only inhibition of binding of an enveloped virus to a cell. The described animal models are clinically relevant. For example, Oberg and Vrang (cited by the Office) describes a simian model similar to that described in the Declaration of February 1, 2001, as resembling HIV injection in humans, and “antiviral drugs have shown activity in this model at dose levels which are effective in humans.” The *only* disadvantages cited by the authors regarding the simian model are cost, the requirement of appropriate facilities, and the need for a substantial amount of the drug to perform the experiments (page 469, col. 2, paragraph 2). The Office has not provided sufficient reasoning to cast doubt on the ability of the isolated and purified antiviral agent of the presently claimed method to inhibit binding of an enveloped virus to a cell in a host, especially in view of the *in vivo* evidence provided.

For the reasons set forth above, the presently claimed invention is enabled by the instant application. Applicant respectfully submits that the Office has not met its burden in setting forth a reasonable explanation disputing the enablement of the presently claimed invention. Therefore, Applicant requests the withdrawal of the rejection under Section 112, first paragraph.

Discussion of Provisional Obviousness-Type Double Patenting Rejection

Claims 20 and 21 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 20-24 of Application No. 09/428,275 (the ‘275 application). Applicant acknowledges the provisional rejection and points out that, in the event the other rejections are withdrawn such that the provisional rejection is the sole remaining rejection, the Office is required to withdraw the rejection in accordance with M.P.E.P. § 804. Alternatively, if the ‘275 application issues as a patent and the rejection is maintained but no longer provisional, Applicant will address the merits of the rejection at that time.

In re Appln. of Boyd
Application No. 09/427,873

Conclusion

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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